Remarks

It is requested that the foregoing Amendment be entered and that the rejections be reconsidered. Claims 1-3, 6-13, 65-68, and 73-74 were examined in this case. Claims 1-3, 6-13, 65-68, and 73-74 were rejected. The present Response amends claims 1, 2, 12, and 74 and cancels claim 3. Each of the objections and rejections issued in the Office Action are addressed individually below.

Support for the Amendment

The amendments to claim 74 and the specification are made to correct typographical errors. Support for the amendments to claims 1 and 2 can be found at page 6, line 16 to page 7, line 2. The present Amendment does not add any new matter to the application.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 67 and 68 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner asserts that there is no original disclosure supporting the recitations in claims 67 and 68 that the biomaterial architecture can be a particle or a nanosphere. Applicant disagrees.

The term "particle" can be found in the specification as filed at page 14, line 20, and page 18, line 23. The term "nanosphere" can be found in the specification as filed at page 10, line 24. Both terms are used in the as filed specification to refer to the biomaterial architecture of the present invention. In light of these facts, withdrawal of this rejection is requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-3, 6-13, 65-68, and 73-74 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. This rejection has multiple aspects, which are addressed individually below.

The Examiner suggests that claim 3 does not limit claim 2. Applicant respectfully traverses this aspect of the rejection. Nonetheless, claim 3 has been canceled and withdrawal of this aspect of rejection is requested.

The Examiner states that there is no antecedent basis for "said biodegradable polymer" in claims 10, 73, and 74. Claim 2, which claims 10, 73, and 74 depend from, has been amended to include "a biodegradable polymer" to provide antecedent basis for claims 10, 73, and 74. Withdrawal of this aspect of the rejection is requested.

The Examiner states that there is no antecedent basis for the phrase "the required specificity" at claim 12, line 2. The phrase "the required" has been deleted from claim 12. Withdrawal of this aspect of the rejection is requested.

Objection to the Claims

The Examiner points out that "is" at claim 74, line 1 should be inserted after polymer. Such amendment has been made and withdrawal of this objection is requested.

Provisional Double Patenting Rejection

Claims 1-3, 6-11, 13, 66, 73, and 74 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-52 of co-pending Application No. 09/600,502. The Examiner states that the '502 application, especially claims 1, 3, 6, and 11, claims the ligand-biotin-avidin or streptavidin-biotin-PLA-PEG structure required for the instant claims.

Applicants will address the double patenting rejection once all other rejections in this case have been withdrawn.

Rejections Under 35 U.S.C. § 102(a)

Claims 1-3, 6-9, 11, 13, and 66 stand rejected under 35 U.S.C. 102(a) as being anticipated by Patel, et al., (FASEB J., Vol. 12, pages 1447-1454) (herein referred to as "Reference R"). A revised Declaration has been submitted, which is sufficient to show that the Patel, et al., reference is not "by another." Applicant thanks the Examiner for reviewing the Declaration before it was submitted to the inventors. In view of the Declaration, Patel, et al., (11/98) is not an anticipatory reference because the invention was not known or used *by others* in this country,

before the invention thereof by the Applicant. Applicant respectfully requests that the Examiner consider the new Declaration and withdraw the rejection under 35 U.S.C. § 102(a).

Claims 1-3, 6-9, 11, 13, and 66-68 stand rejected under 35 U.S.C. 102(a) as being anticipated by Cannizzaro, et al., (Biotechnol. Bioeng. Vol. 58, pages 529-535) (herein referred to as "Reference S"). Applicant submits herewith a Declaration, which is sufficient to show that the Cannizzaro, et al., reference is not "by another." Again, Applicant thanks the Examiner for reviewing the Declaration before it was submitted to the inventors. In view of the Declaration, Cannizzaro, et al., (6/5/98) is not an anticipatory reference because the invention was not known or used *by others* in this country, before the invention thereof by the Applicant. Applicant respectfully requests that the Examiner consider the Declaration and withdraw the rejection under 35 U.S.C. § 102(a).

Rejections Under 35 U.S.C. § 102(b)

Claims 2, 3, 8, and 13, stand rejected under 35 U.S.C. 102(b) as being anticipated by Davies, et al., (Langmuir, Vol 10, pages 2654-2661). The Examiner states on page 7-8 of the Office Action that the Davies, et al., article is not applied against instant claim 1, which requires a biodegradable polymer. Claim 2 has been amended to recite a biodegradable polymer. Therefore, the Davies, et al., reference does not apply and this rejection should be withdrawn.

Claims 1-3, 6-8, 10, 11, 13, 66, 73, and 74 were rejected under 35 U.S.C. 102(b) as being anticipated by Boyce (U.S. Patent No. 5,273,900) (herein referred to as "Boyce"). The Examiner asserts that collagen is a polyamide and a polyprotein and that Boyce teaches biotinylated collagen that is attached to a biotinylated biologically active molecule through avidin, which corresponds to Applicant's anchor-adapter-tag unit. Applicant disagrees.

Independent claim 1 recites a composition comprising a biodegradable polymer having a ligand attached thereto, wherein said ligand is attached to said biodegradable polymer via an anchor-adapter-tag unit comprising an anchor incorporated into the polymer and through which the unit is retained on the polymer, a tag attached to the ligand, and an adapter that links the anchor and the tag. Independent claim 2 recites a composition comprising a biomaterial architecture having a ligand attached thereto through a biomolecular interaction, wherein said

biomaterial architecture comprises a biodegradable polymer having an anchor moiety incorporated therein, and wherein said biomolecular interaction is effected by an anchor-adapter-tag unit comprising the anchor, a tag attached to the ligand, and an adapter that links the anchor and the tag, wherein the unit is retained on the polymer by the anchor.

As recited in the claims, the invention relates to a biomaterial architecture comprising a polymer having an anchor moiety *incorporated therein* to facilitate recognition events for the attachment of ligands to the biomaterial architecture. As stated in the specification,

> "an anchor moiety must first be *incorporated into* the biomaterial architecture. The biomaterial architecture can be fabricated from any biodegradable and bioresorbable material that is capable of having an anchor moiety incorporated therein..... Once the polymer is selected, this polymer material can be contacted with a desired anchor material to form a polymer-anchor material. " (page 6, line 19 to page 7, line 2).

As stated in the claims, the biodegradable polymer has an anchor moiety incorporated therein. The ability to effectively attach ligands onto the polymer surface via biomolecular interactions is particularly useful for the *post-fabrication* modification of architecture surfaces. It is often difficult to effect post-fabrication attachment of ligands to certain biomaterial architectures via covalent interactions due to the harsh conditions required for covalent attachment. Such harsh conditions can compromise the biomaterial architecture. For example, surfactants can mask available functional groups on the architecture surface. Significantly, Applicant's polymer composition allows for the attachment of ligands to biomaterial architectures using mild conditions that will not compromise the biomaterial architectures.

Nowhere does Boyce disclose the incorporation of anchor molecules into a polymer for attachment of a ligand. What Boyce does disclose is attachment of ligands to a pre-fabricated polymer surface by 1) "covalent binding" or 2) "conjugation" (which also utilizes covalent binding). The dermal membrane component is first prepared from collagen and a mucopolysaccharide such as glycosaminoglycan (GAG) (see column 7, lines 7-12). The dermal membrane component is then preferably surface-laminated using a biopolymeric material (column 7, lines 12-16). Biologically active molecules are then attached to the surface-laminated dermal membrane component. In "covalent binding," the biologically active molecules are directly covalently bound to the surface-laminated dermal membrane component. In "conjugation," the biologically active molecules are indirectly associated with a second molecule

that is covalently bound to the surface-laminated dermal membrane component. As an example of conjugation, Boyce discloses that "biotin may be covalently bound to a biopolymer of the dermal component of the skin replacement, such as collagen, so that the collagen becomes 'biotinylated.' The biotinylated collagen is then conjugated with a polyconjugal protein, avidin, which in turn has been covalently bound to a biologically active molecule" (column 10, lines 22-28).

With techniques such as those described by Boyce, covalent linkage in the post-processing step, that is, after the biomaterial architecture has been fabricated, may compromise the biomaterial architecture. As described in the specification, Applicant's composition of polymers having an anchor incorporated therein, which is then available on the surface of the architecture to enable surface modification, represents a significant improvement in the fabrication and modification of the surfaces of biomaterial architectures because mild reaction conditions can be utilized. These inventive techniques can be applied to a wide range of ligands and a number of applications, for example tissue engineering or drug delivery applications. In contrast, Boyce relies on traditional methods, which are known in the art to interfere with ligand attachments and many biomaterial applications.

Anticipation under 35 U.S.C. 102 requires that the invention disclosed by the prior art reference must be identical to the claimed invention in each and every aspect. As stated in *Hybritech Inc. v. Monoclonal Antibodies, Inc,* 802 F.2d 1367,231 U.S.P.Q. 81 (Fed. Cir. 1986), "[I]t is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention." Nowhere do Boyce, et al., teach of an anchor molecule that is *incorporated into* a polymer for attachment of a ligand as presently claimed. Therefore, the Boyce reference does not anticipate the claimed invention and withdrawal of this rejection under 35 U.S.C. § 102(b) is requested.

Claims 1-3, 6-8, 10, 11, 13, 66-68, 73, and 74 were rejected under 35 U.S.C. § 102(b) as being anticipated by Li, et al. (U.S. Patent No. 5,512,294). The Examiner states that polymerized liposomes correspond to Applicant's biodegradable polymer; the biotin groups attached to the polymerized liposomes correspond to Applicant's anchor; the avidin or streptavidin correspond to Applicant's adapter; and the biotinylated antibodies correspond to Applicant's tag-ligand. Applicant disagrees.

Independent claim 1 recites a composition comprising a biodegradable polymer having a ligand attached thereto, wherein said ligand is attached to said biodegradable polymer via an anchor-adapter-tag unit comprising an anchor incorporated into the polymer and through which the unit is retained on the polymer, a tag attached to the ligand, and an adapter that links the anchor and the tag. Independent claim 2 recites a composition comprising a biomaterial architecture having a ligand attached thereto through a biomolecular interaction, wherein said biomaterial architecture comprises a biodegradable polymer having an anchor moiety incorporated therein, and wherein said biomolecular interaction is effected by an anchor-adapter-tag unit comprising the anchor, a tag attached to the ligand, and an adapter that links the anchor and the tag, wherein the unit is retained on the polymer by the anchor.

As recited in the claims, the anchor moiety incorporated into the biodegradable polymer (see page 6, line 19 to page 7, line 2). Like Boyce, Li, et al., lacks any teaching of incorporation of anchor molecules into a polymer for attachment of a ligand. In contrast, Li, et al., teach of a of a "biotinylated antibody-avidin conjugate" (anchor) which is attached to a "polymerized liposome" (polymer) only after the polymer is made (column 9, lines 12-13). That is, the biotinylated antibody-avidin conjugate is not incorporated into the polymer during polymerization, but is attached to the polymer in a post-processing step. Nowhere do Li, et al., teach anchor molecules that are incorporated into a polymer.

Anticipation under 35 U.S.C. 102 requires that the invention disclosed by the prior art reference must be identical to the claimed invention in each and every aspect. As stated in *Hybritech Inc. v. Monoclonal Antibodies, Inc,* 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986), "[I]t is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention." Since attachment of the anchor occurs in the post-processing step, Li, et al., cannot anticipate the claimed invention. Withdrawal of this rejection under 35 U.S.C. § 102(b) is requested.

Rejections Under 35 U.S.C. § 102(e)

Claims 1-3, 6-9, 11, 13, 65, 67, and 68 stand rejected under 35 U.S.C. 102(e) as being anticipated by Hirosue, et al. The Examiner states that Hirosue, et al., teach biodegradable polymer nanospheres encapsulating therapeutic nucleic acids. The Examiner further states that

the nanospheres can be biotinylated, and avidin can be used as a bridge for attachment of biotinylated ligands. Applicant disagrees.

Independent claim 1 recites a composition comprising a biodegradable polymer having a ligand attached thereto, wherein said ligand is attached to said biodegradable polymer via an anchor-adapter-tag unit comprising an anchor incorporated into the polymer and through which the unit is retained on the polymer, a tag attached to the ligand, and an adapter that links the anchor and the tag. Independent claim 2 recites a composition comprising a biomaterial architecture having a ligand attached thereto through a biomolecular interaction, wherein said biomaterial architecture comprises a biodegradable polymer having an anchor moiety incorporated therein, and wherein said biomolecular interaction is effected by an anchor-adapter-tag unit comprising the anchor, a tag attached to the ligand, and an adapter that links the anchor and the tag, wherein the unit is retained on the polymer by the anchor.

The instant claims pertain to polymers having anchor moieties incorporated therein. The anchor moieties are available on the interior and on the surface of the polymer. In contrast, as with Boyce and Li, et al., Hirosue, et al., lack any teaching of an anchor incorporated into a polymer. Hirosue, et al., teach of "targeting molecules" that can be attached to a polymer in a post-processing step using traditional methods known in the art to interfere with ligand attachment and many biomaterials applications. Specifically, Hirosue, et al., states that "targeting moieties are attached to the *surface* of the nanospheres" (column 4, lines 18-26). In one embodiment Hirosue, et al., disclose that the targeting moiety can be attached by covalent linkage directly to the particle surface (column 4, lines 28-30). For example, Hirosue, et al., disclose that biotin is covalently attached to the polymer (column 4, lines 33-36). Hirosue, et al., do not teach incorporation of an anchor moiety within a biodegradable polymer, but instead assert that covalent attachment can be used to link anchor molecules to the surface of a nanosphere after the processing of the nanosphere has already occurred (column 4, lines 28-36). Nowhere do Hirosue, et al., disclose polymers having anchor moieties incorporated therein.

In light of the above distinctions, Applicant submits that the Hirosue, et al., reference does not contain every element of the claimed invention, and thus is not anticipatory under 35 U.S.C. § 102(b). Applicant respectfully requests withdrawal of this rejection.

Conclusion

Based on the arguments presented above, it is submitted that the pending claims, as amended herein, are allowable over the art of record. Applicant would like to thank the Examiner for thoughtful comments and careful consideration of the case. If a telephone conversation would help expedite prosecution of this case, please do not hesitate to contact the undersigned at (617) 248-5000.

Please charge any fees that may be required, or credit any overpayment, to our Deposit Account No. 03-1721.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313
on June 9, 2003